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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,692	11/16/2000	Kuo-Fen Lee	D6233CIP	5372
7590 03/04/2004			EXAMINER	
Benjamin Aaron Adler McGregor & Adler LLP 8011 Candle Lane Houston, TX 77071			BUNNER, BRIDGET E	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/714,692	<b>Applicant(s)</b> LEE ET AL.	
	<b>Examiner</b> Bridget E. Bunner	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 20-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Application, Amendments and/or Claims***

The amendment 05 December 2003 has been entered in full. Claims 1-19 and 24-27 are cancelled.

The Examiner acknowledges that Applicant requests the fees paid for the Notice of Appeal and Appeal Brief be credited to the appropriate deposit account. However, Applicant must separately request the refund in writing and address it to the attention of Ms. Margaret Stevens.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 20-23 are under consideration in the instant application.

### ***Claim Rejections - 35 USC § 102***

1. Claims 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Villalona-Calero et al. (Ann Oncol 9: 71-77, 1998). The basis for this rejection is set forth at pg 2-3 of the previous Office Action (21 October 2003).

Applicant's arguments (Paper No. 14, 20 November 2001), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that Villalona-Calero et al. do not teach or suggest a method of using corticotrophin releasing factor to inhibit angiogenesis in a target tissue as claimed. Applicant contends that Villalona-Calero et al. do not teach or suggest any relationship between

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angiogenesis and the prevention of vascular leakage, and one of ordinary skill in the art would readily recognize that these are two distinct biological processes.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action, Villalona-Calero et al. teaches that patients with primary or secondary brain tumors with evidence of edema are administered a CRFR2 agonist (human corticotropin-releasing factor (hCRF)) intravenously, by continuous infusion (pg 72, col 1, first and second full paragraphs). Villalona-Calero et al. discloses that hCRF reduces water content in tumor and peritumoral tissue in brain tumor models *in vivo* when administered subcutaneously (pg 72, col 1; pg 76, first paragraph). Villalona-Calero et al. also indicates that this effect is a direct action on the tumor microvasculature (pg 76, first paragraph). However, since Villalona-Calero et al. administers human corticotrophin releasing factor (a CRFR2 agonist) to the same subject population and the same tissues as recited in the claims, inhibition of angiogenesis must have been inherently occurring in the prior art of Villalona-Calero et al. (Ex parte Novitski, 26 USPQ2d 1389 (BPAI 1993). Villalona-Calero et al.'s disclosure fully meets the terms of the claimed method because a CRFR2 agonist (corticotropin releasing factor) inherently possesses angiogenesis-inhibiting activity.

(ii) Applicant also argues that Villalona-Calero et al. do not teach or suggest anything related to the uses of urocortin. Applicant indicates that Villalona-Calero et al. do not provide one of ordinary skill in the art with any reasonable and logical basis to use urocortin or corticotrophin releasing factor to inhibit angiogenesis in a target tissue as claimed. Applicant concludes that

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Villalona-Calero et al. do not anticipate the instant invention because Villalona-Calero et al. do not teach or suggest each and every aspect of the present invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Although Villalona-Calero et al. does not teach the administration of urocortin to a target tissue, Villalona-Calero et al. teaches the administration of human corticotrophin releasing factor (hCRF; a CRFR2 agonist) to patients with primary or secondary brain tumors with evidence of edema (pg 72, col 1, first and second full paragraphs). Villalona-Calero et al. also discloses that hCRF reduces water content in tumor and peritumoral tissue in brain tumor models *in vivo* when administered subcutaneously (pg 72, col 1; pg 76, first paragraph). Although Applicant claims that Villalona-Calero et al. does not teach anything related to the uses of urocortin, claim 21 recites that the CRFR2 agonist is selected from the group consisting of urocortin *and* corticotrophin releasing factor. Since claim 21 requires that either urocortin or corticotrophin releasing factor be administered, Villalona-Calero et al. satisfies the claim requirement by the administration of hCRF. As mentioned above, Villalona-Calero et al. teaches each and every aspect of the present invention because human corticotrophin releasing factor (a CRFR2 agonist) is administered to the same subject population and to the same tissues as recited in the claims. Additionally, CRFR2 agonist (corticotrophin releasing factor) inherently possesses angiogenesis-inhibiting activity.

***Conclusion***

No claims are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Elizabeth C. Kemmerer*

BEB  
Art Unit 1647  
27 February 2004

ELIZABETH KEMMERER  
PRIMARY EXAMINER